

TYPHOID FEVER (notifiable as *SALMONELLOSIS*)

DISEASE REPORTING

In Washington

DOH receives 2 to 8 reports of typhoid fever per year.

Cases are most often associated with travel as typhoid is no longer endemic to Washington. Common exposures include contaminated food (including shellfish and fruit) and water.

Purpose of reporting and surveillance

- To identify sources of transmission (e.g., a commercial product or food handler) and to prevent further transmission from such sources.
- To identify cases or carriers that may be a source of infection for other persons (for example, a food handler) and to prevent further transmission from such sources.
- To educate potentially exposed persons about the signs and symptoms of disease to facilitate early diagnosis.

Reporting requirements

- Health care providers: **immediately notifiable to Local Health Jurisdiction**
- Hospitals: **immediately notifiable to Local Health Jurisdiction**
- Laboratories: notifiable within 2 workdays; specimen submission required
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

An illness caused by *Salmonella typhi* that is often characterized by insidious onset of sustained fever, headache, malaise, anorexia, relative bradycardia, constipation or diarrhea, and nonproductive cough. However, many mild and atypical infections occur. Carriage of *S. typhi* may be prolonged.

Laboratory criteria for diagnosis

- Isolation of *S. typhi* from blood, stool, or other clinical specimen.

Case definition

- Probable: a clinically compatible case that is epidemiologically linked to a confirmed case in an outbreak.
- Confirmed: a clinically compatible case that is laboratory confirmed.

Isolation of the organism is required for confirmation. Serologic evidence alone is not sufficient for diagnosis. Asymptomatic carriage should not be reported as typhoid fever. Isolates of S. typhi are reported to the Foodborne and Diarrheal Diseases Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases, CDC, through the Public Health Laboratory Information System.

A. DESCRIPTION**1. Identification**

Systemic bacterial diseases characterized by insidious onset of sustained fever, severe headache, malaise, anorexia, a relative bradycardia, splenomegaly, rose spots on the trunk in 25% of white patients, nonproductive cough in the early stage of the illness and constipation more commonly than diarrhea in adults. Many mild and atypical infections occur.

In typhoid fever, ulceration of Peyer patches in the ileum can produce intestinal hemorrhage or perforation (about 1% of cases), especially late in untreated cases. Severe forms have been described with cerebral dysfunction. Nonsweating fever, mental dullness, slight deafness and parotitis may occur. The case-fatality rate of 10%-20% observed in the preantibiotic era can be reduced to less than 1% with prompt antibiotic therapy. Depending on the antimicrobial agent used, (15%-20%) of patients may experience relapses (which are generally much milder than the initial clinical illness). Mild and inapparent illnesses occur, especially in endemic areas.

A new nomenclature for *Salmonella* has been proposed based on DNA relatedness. According to the proposed nomenclature, only two species would be recognized- *Salmonella bongori* and *Salmonella enterica* (both genus and species italicized). All human pathogens would be regarded as serovars within subspecies I of *S. enterica*. The proposed nomenclature would change *S. typhi* to *S. enterica* serovar Typhi, abbreviated *S. Typhi* (note that Typhi is not italicized and a capital letter is used.) Some official agencies have adopted the new nomenclature although it had not been officially approved as of mid-1999. This new nomenclature is used in this chapter.

Paratyphoid fever presents a similar clinical picture, but tends to be milder, and the case-fatality rate is much lower. The ratio of disease caused by *Salmonella enterica* serovar Typhi (*S. Typhi*) to that caused by *S. enterica*, serovar Paratyphi A and B (*S. Paratyphi A*, *S. Paratyphi B*) is about 10:1. Relapses may occur in approximately 3%-4% of cases. When the *Salmonella* infections are not systemic, they are manifested only by a gastroenteritis (see Salmonellosis).

The etiologic organisms can be isolated from the blood early in the disease and from urine and feces after the first week; bone marrow culture provides the best bacteriologic confirmation (90%-95% recovery) even in patients who have already received antimicrobials. Because of its limited sensitivity and specificity, serologic tests (widal test) are generally of little diagnostic value.

2. Infectious Agent

For typhoid fever, *S. Typhi*, the typhoid bacillus. Phage typing and pulsed field gel electrophoresis of *S. Typhi* are valuable laboratory tests for characterizing isolates in epidemiologic studies.

For paratyphoid fever, three serovars of *S. enterica* are recognized: *S. Paratyphi A*, *S. Paratyphi B*, and *S. Paratyphi C*. A number of phage types can be distinguished.

3. Worldwide Occurrence

Worldwide; the annual incidence of typhoid fever is estimated at about 17 million cases with approximately 600,000 deaths. The number of sporadic cases of typhoid fever has remained relatively constant in the US, with fewer than 500 cases annually for several years (compared with 2,484 reported in 1950), and, with development of sanitary facilities, has been virtually eliminated from many areas; most US cases now are imported from endemic areas. Strains resistant to chloramphenicol and other recommended antimicrobials have become prevalent in several areas of the world. The majority of isolates from south and southeast Asia, the Middle East and northeast Africa in the 1990s have been strains carrying an R factor plasmid that encodes resistance to multiple antimicrobial agents that were previously the mainstays of oral therapy including chloramphenicol, amoxicillin and trimethoprim/sulfamethoxazole.

Paratyphoid fever occurs sporadically or in limited outbreaks, probably more frequently than reports suggest. In the US and Canada, paratyphoid fever is infrequently identified. Of the three bioserotypes, paratyphoid B is most common, A less frequent and C extremely rare.

4. Reservoir

Humans for both typhoid and paratyphoid; rarely, domestic animals for paratyphoid. Family contacts may be transient or permanent carriers. In most parts of the world, short-term fecal carriers are more common than urinary carriers. The carrier state may follow acute illness or mild or even subclinical infections. The chronic carrier state is most common among persons infected during middle age, especially women; carriers frequently have biliary tract abnormalities including gallstones. The chronic urinary carrier state occurs in those with schistosome infections. In one outbreak of paratyphoid fever in England, dairy cows excreted Paratyphi B organisms in milk and feces.

5. Mode of Transmission

By food and water contaminated by feces and urine of patients and carriers. Important vehicles in some countries include shellfish taken from sewage contaminated beds (particularly oysters), raw fruits, vegetables fertilized by night soil and eaten raw, contaminated milk and milk products (usually contaminated by hands of carriers) and missed cases. Flies may infect foods in which the organism then multiplies to achieve an infective dose, which is much lower for typhoid than for paratyphoid bacteria.

6. Incubation period

The incubation period depends on the size of the infecting dose; from 3 days to 1 month with a usual range of 8-14 days. For paratyphoid gastroenteritis, 1-10 days.

7. Period of communicability

As long as the bacilli appear in excreta, usually from the first week throughout convalescence; variable thereafter (commonly 1-2 weeks for paratyphoid). About 10% of untreated typhoid fever patients will discharge bacilli for 3 months after onset of symptoms, and 2%-5% become permanent carriers; considerably fewer persons infected with paratyphoid organisms may become permanent gallbladder carriers.

8. Susceptibility and resistance

Susceptibility is general and is increased in individuals with gastric achlorhydria or those who are HIV positive. Relative specific immunity follows recovery from clinical disease, inapparent infection and active immunization. In endemic areas, typhoid fever is most common in preschool and children 5-19 years of age.

B. METHODS OF CONTROL**1. Preventive measures:**

- a. Educate the public regarding the importance of handwashing. Provide suitable handwashing facilities; this is particularly important for food handlers and attendants involved in the care of patients and children.
- b. Dispose of human feces in a sanitary manner and maintain fly proof latrines. Stress use of sufficient toilet paper to minimize finger contamination. Under field conditions, dispose of feces by burial at a site distant and downstream from the source of drinking water.
- c. Protect, purify and chlorinate public water supplies, provide safe private supplies, and avoid possible back flow connections between water and sewer systems. For individual and small group protection, and while traveling or in the field, treat water chemically or by boiling.

- d. Control flies by screening, spraying with insecticides and use of insecticidal baits and traps. Control fly breeding by frequent collection and disposal of garbage, and fly control measures in latrine construction and maintenance.
- e. Use scrupulous cleanliness in food preparation and handling; refrigerate as appropriate. Particular attention should be directed to the proper storage of salads and other foods served cold. These provisions apply equally to home and public eating places. If uncertain about sanitary practices, select foods that are cooked and served hot, and fruits peeled by the consumer.
- f. Pasteurize or boil all milk and dairy products. Supervise the sanitary aspects of commercial milk production, storage and delivery.
- g. Enforce suitable quality-control procedures in industries that prepare food and drink for human consumption. Use chlorinated water for cooling during canned food processing.
- h. Limit the collection and marketing of shellfish to supplies from approved sources. Boil or steam (for at least 10 minutes) before serving.

Instruct patients, convalescents and carriers in personal hygiene. Emphasize handwashing as a routine practice after defecation and before preparing and serving food.

- i. Encourage breast feeding throughout infancy; boil all milk and water used for infant feeding.
- j. Exclude typhoid carriers from handling food and from providing patient care. Identify and supervise typhoid carriers; culture of sewage may help in locating carriers. Chronic carriers should not be released from supervision and restriction of occupation until local or state regulations are met, often not until 3 consecutive negative cultures are obtained from authenticated fecal (and urine in schistosomiasis endemic areas) specimens taken at least 1 month apart and at least 48 hours after antimicrobial therapy has stopped. Fresh stool specimens are preferred to rectal swabs; at least 1 of the 3 consecutive negative stool specimens should be obtained by purging.

In recent studies, the new oral quinolones have produced excellent results in the treatment of the carrier, even when biliary disease exists; follow-up cultures are necessary to confirm cure.

- k. Typhoid fever: Immunization is not routinely recommended in the US. Current practice is to immunize those subject to unusual exposure to enteric infections from occupation (e.g., clinical microbiology technicians) or travel to endemic areas, those living in areas of high endemicity, and household members of known carriers. An oral, live vaccine using *S. Typhi* strain Ty21a (requiring 3 or 4 doses, 2 days apart) and a parenteral vaccine containing the polysaccharide Vi antigen (single dose) are available. Since these vaccines are as protective as the whole cell bacteria vaccine and are much less reactogenic, they are the vaccines of choice. However, Ty21a should not be used in patients receiving antibiotics or the antimalarial mefloquine. Because it commonly elicits marked systemic adverse reactions, use of the old inactivated whole cell vaccines is strongly discouraged. Booster doses are desirable for those at continuing risk of infection with an interval between booster doses ranging from 2 to 5 years, depending on the type of vaccine.

Paratyphoid fever: In field trials, oral typhoid vaccine (Ty21a) conferred partial protection against paratyphoid B but not as well as it protected against typhoid.

2. Control of patient, contacts and the immediate environment:

- a. Report to local health authority.
- b. Isolation: Enteric precautions while ill; hospital care is desirable during acute illness. Release from supervision by local health authority should be based on not fewer than 3 consecutive negative cultures of feces (and urine in patients with schistosomiasis) taken at least 24 hours apart and at least 48 hours after any antimicrobials, and not earlier than 1 month after onset; if any one of these is positive, repeat cultures at intervals of 1 month during the 12 months following onset until at least 3 consecutive negative cultures are obtained.
- c. Concurrent disinfection: Of feces and urine and articles soiled therewith. In communities with modern and adequate sewage disposal systems, feces and urine can be disposed of directly into sewers without preliminary disinfection. Terminal cleaning.
- d. Quarantine: None.
- e. Immunization of contacts: Routine administration of typhoid vaccine is of limited value for family, household and nursing contacts who have been or may be exposed to active cases; it should be considered for those who may be exposed to carriers. There is no effective immunization for paratyphoid A fever.
- f. Investigation of contacts and source of infection: The actual or probable source of infection of every case should be determined by search for unreported cases, carriers or contaminated food, water, milk or shellfish. All members of travel groups in which a case has been identified should be followed.

The presence of elevated antibody titers to purified Vi polysaccharide is highly suggestive of the typhoidal carrier state. Identification of the same phage type in the organisms isolated from patients and a carrier suggests a possible chain of transmission.

Household and close contacts should not be employed in sensitive occupations (e.g., food handlers) until at least 2 negative feces and urine cultures, taken at least 24 hours apart, are obtained.

- g. Specific treatment: Increasing prevalence of resistant strains currently dictates therapy. In general, in adults, oral ciprofloxacin should be considered the drug of choice, particularly in patients from Asia. There have been recent reports of Asian strains showing diminished in vivo sensitivity. If local strains are known to be sensitive, oral chloramphenicol, amoxicillin or TMP-SMX (particularly in children) have comparable high efficacy for acute infections. Ceftriaxone is a parenteral once daily antibiotic that is useful in obtunded patients or those with complications in whom oral antibiotics cannot be used. Short-term, high dose corticosteroid treatment, combined with specific antibiotics and supportive care, clearly reduce mortality in critically ill patients. (See B1j, above, for treatment of the carrier state.) Patients with concurrent schistosomiasis must also be treated with praziquantel to eliminate possible carriage of *S. Typhi* bacilli by the schistosomes.

3. Epidemic measures

- a. Search intensively for the case or carrier who is the source of infection and for the vehicle (water or food) by which infection was transmitted.
- b. Selectively eliminate suspected contaminated food.
- c. Pasteurize or boil milk, or exclude milk supplies and other foods suspected on epidemiologic evidence, until safety is ensured.
- d. Chlorinate suspected water supplies adequately under competent supervision or avoid use. All drinking water must be chlorinated, treated with iodine or boiled before use.
- e. Routine use of vaccine is not recommended.

4. International measures

- a. For typhoid fever: Immunization is advised for international travelers to endemic areas, especially if travel will likely involve exposure to unsafe food and water, or close contact in rural areas to indigenous populations. Immunization is not a legal requirement for entry into any country.
- b. For both typhoid and paratyphoid fevers, WHO Collaborating Centres.

